EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Applicant's representative, H. James Voeller, on December 30, 2009.

The application has been amended as follows:

ENTER the new claim listing:

1-16. (cancelled)

17. (currently amended) A multimeric molecule, corresponding to the following general formula:

$A–X_n$

wherein:

n is equal to 3, 4, 5 or 6,

A is a chemical moiety, functionalized by at least three amino functions or COOH functions or SH functions or

S-Npys (S-nitro-pyridinesulphenyl) functions or S-Pys

(S-pyridinesulphenyl) functions, and

X represents a -D, -B-D, or -B(D)-D' group, in which:

B is a spacer arm, and

-D and -D' each represent a peptide corresponding to a sequence derived from a ligand, chosen from the residues forming the interface with the ligand receptor, said sequence capable of interacting with the receptor, said ligand being CD40L.

18. (previously presented) The molecule of claim 17, wherein -D and -D' each represent a peptide derived from the ligand of the human or murine CD40 receptor (CD40L), each said peptide belonging to the primary sequence of the CD40L and comprising between 3 and 10 amino acids.

19. (currently amended) The molecule of claim 17, wherein each peptide derived from the ligand of the human or murine CD40 receptor (CD40L) is chosen from the following:

Lys-Gly-Tyr (SEQ ID NO: 1),

Tyr-Gly-Lys (SEQ ID NO: 2),

Lys-Gly-Tyr-Tyr (SEQ ID NO: 3),

Tyr-Tyr-Gly-Lys (SEQ ID NO: 4),

Lys-Pro-Arg (SEQ ID NO: 5),

Arg-Phe-Glu-Arg-Ile-Leu-Leu-Arg (SEQ ID NO: 6),

Arg-Leu-Leu-Ile-Arg-Glu-Phe-Arg (SEQ ID NO: 7),

Arg-Phe-Glu-Arg-Ile (SEQ ID NO: 25),

Ile-Arg-Glu-Phe-Arg (SEQ ID NO: 9),

Arg-Ile-Leu-Leu-Arg (SEQ ID NO: 10),

Arg-Leu-Leu-Ile-Arg (SEQ ID NO: 11),

Cys-Gly-Gln-Gln-Ser-Ile (SEQ ID NO: 12),

Ile-Ser-Gln-Gln-Gly-Cys (SEQ ID NO: 26),

Gly-Ser-Glu-Arg-Ile-Leu-Leu-Lys (SEQ ID NO: 14),

Lys-Leu-Leu-Ile-Arg-Glu-Ser-Gly (SEQ ID NO: 15),

Gly-Ser-Glu-Arg-Ile (SEQ ID NO: 16),

Ile-Arg-Glu-Ser-Gly (SEQ ID NO: 17),

Arg-Ile-Leu-Leu-Lys (SEQ ID NO: 18),

Lys-Leu-Leu-Ile-Arg (SEQ ID NO: 19),

Cys-Glu-Gln-Gln-Ser-Val (SEQ ID NO: 20), or

Val-Ser-Gln-Gln-Glu-Cys (SEQ ID NO: 21),

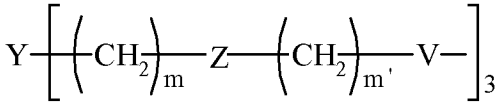
or from hybrid peptides ~~constituted by~~ comprising at least two consecutive amino acids of two of the sequences defined above,

or from fragments of said peptides and hybrid peptides, the amino acids being equally able to be of L or D-configuration.

20. (previously presented) The molecule of claim 17, wherein A has a C_3 symmetry.

21. (previously presented) The molecule of claim 17, wherein:

either A is a branched radical with C_3 symmetry with the following general formula:



in which:

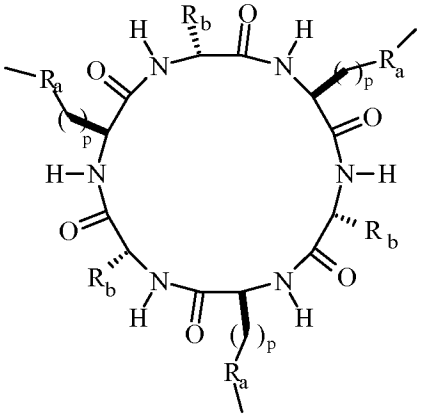
m and m' are integers comprised from 1 to 5,

V represents an -NH- or -CO- group forming an amide bond with X,

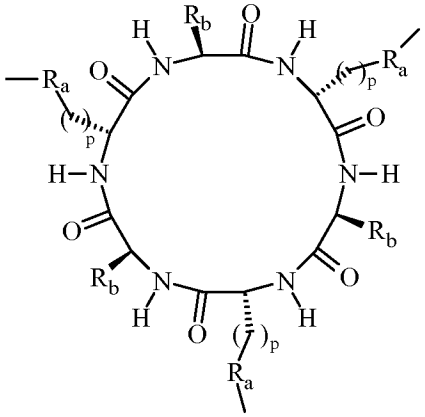
Z represents an oxygen atom or a CH2 group, and

Y represents either a nitrogen atom, or an R-C- group or an R-CONH-C- group, in which R can be an alkyl group with 1 to 10 carbon atoms, an alkenyl group with 1 to 10 carbon atoms, an alkynyl group with 1 to 10 carbon atoms, an aryl group with 5 to 12 carbon atoms, an aralkyl group with 5 to 14 carbon atoms or a heteroaryl group with 1 to 10 carbon atoms, said groups are capable of being non-substituted or substituted by 1 to 6 substituents chosen from the -COOH, -NH2, -CONH2 or alkoxy groups,

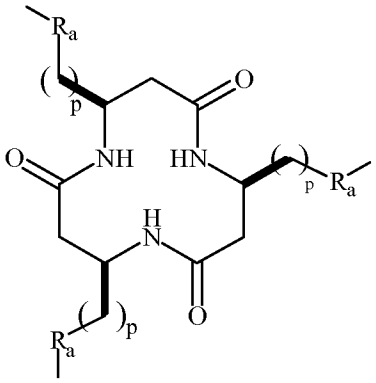
or A is a cyclic C3 radical corresponding to one of the following general formulae:



Ia



Ib



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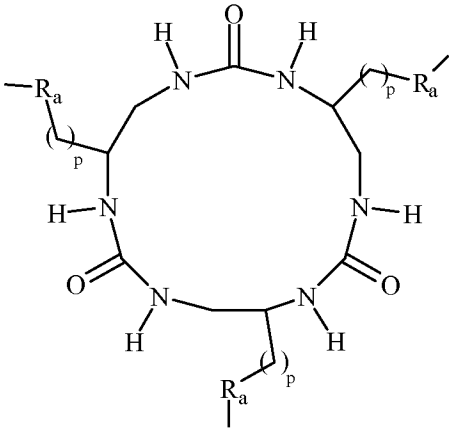

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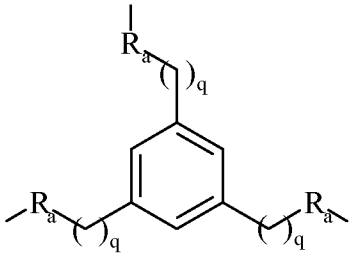

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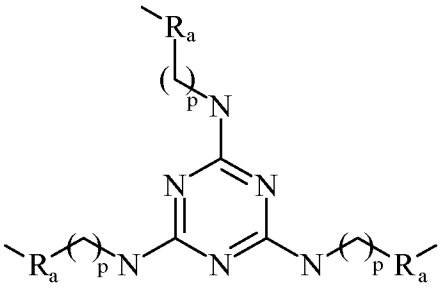
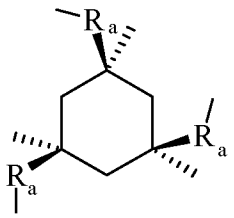
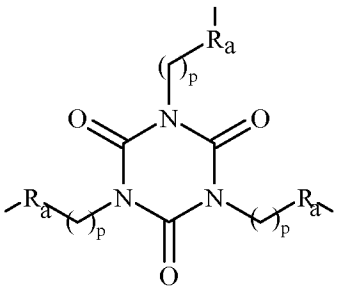


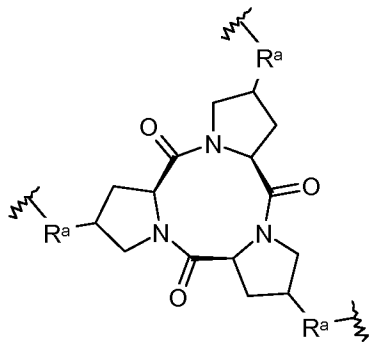
V



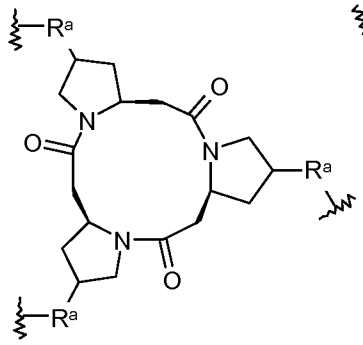
VI



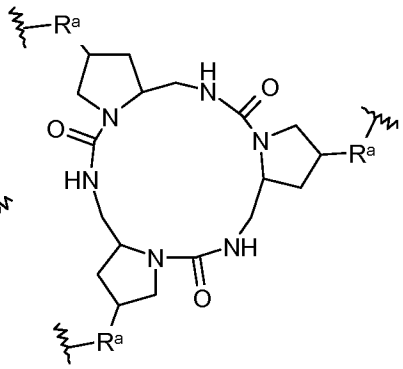
VIa



VIb



VIc



VId

in which:

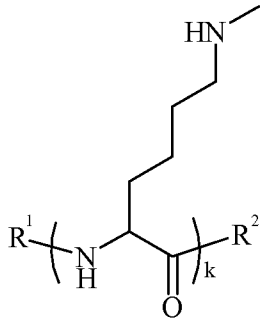
R_a represents either an -NH- group or a -CO- group forming an amide bond with X,

R_b represents the side chain of a proteinogenic amino acid,

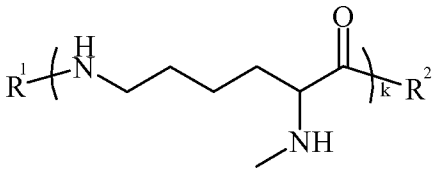
p is an integer comprised from 1 to 4, and

q is an integer comprised from 0 to 4,

or A is a non-symmetrical branched radical corresponding to the following general formulae:



VII



VIII

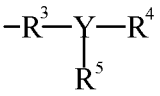
in which:

k represents 3, 4, 5 or 6,

R^1 represents either a hydrogen atom, or an amino acid residue chosen from the proteinogenic amino acids, or an RCO-, ROCO- or RNHCO- group, R being as defined above,

R^2 represents either an $-NH_2$ group, or an -NHR group, or an amino acid residue chosen from the proteinogenic amino acids, R being as defined above, and

B corresponds to one of the following general formulae:

$-R^3-Y-R^4$ or 

in which:

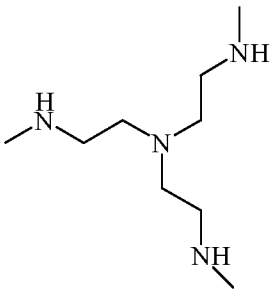
Y represents a C_1-C_{10} alkyl chain or an alkynyl or alkenyl or aryl or aralkyl or heteroaryl group,

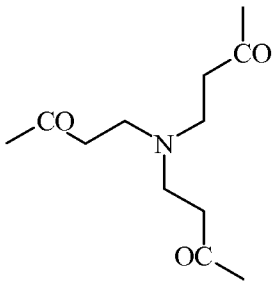
R^3 represents either an -NH- group when V or R_a is a -CO- group, or a -CO- group when V or R_a is an -NH- group,

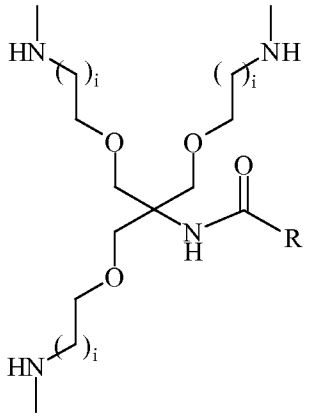
R^4 and R^5 represent independently of one another a -CO- group or an -NH- group, and

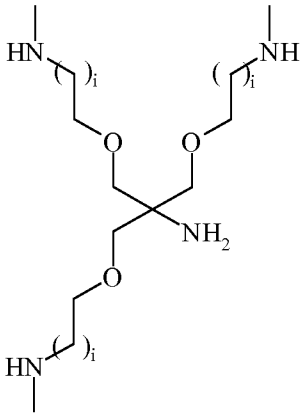
-D and -D' are each a peptide as defined in claim 17.

22. (Withdrawn) The molecule of claim 17, wherein A corresponds to one of the following formulae:



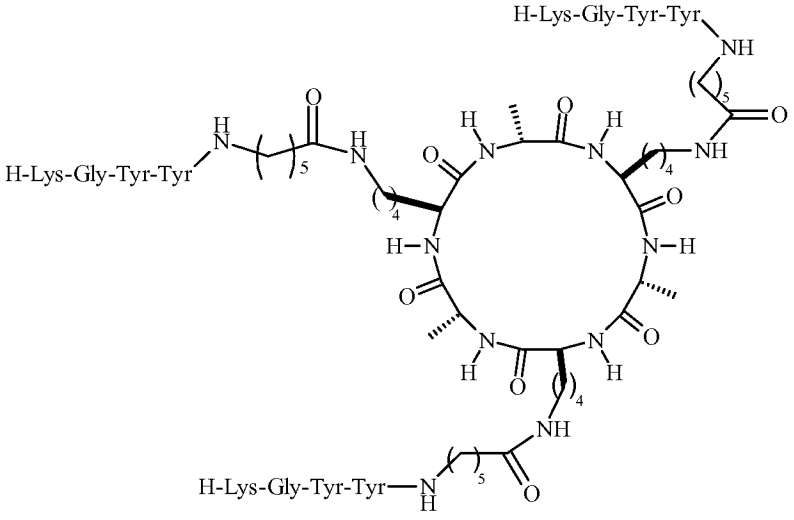


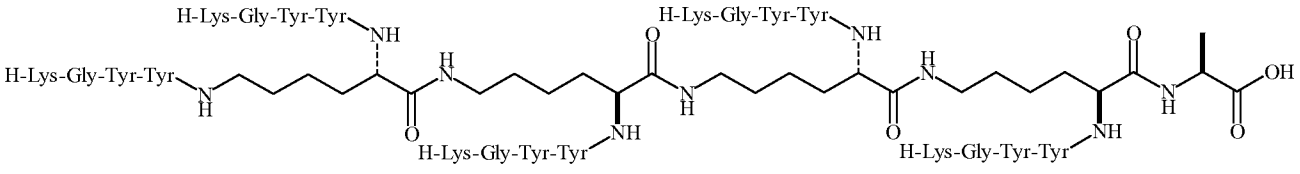


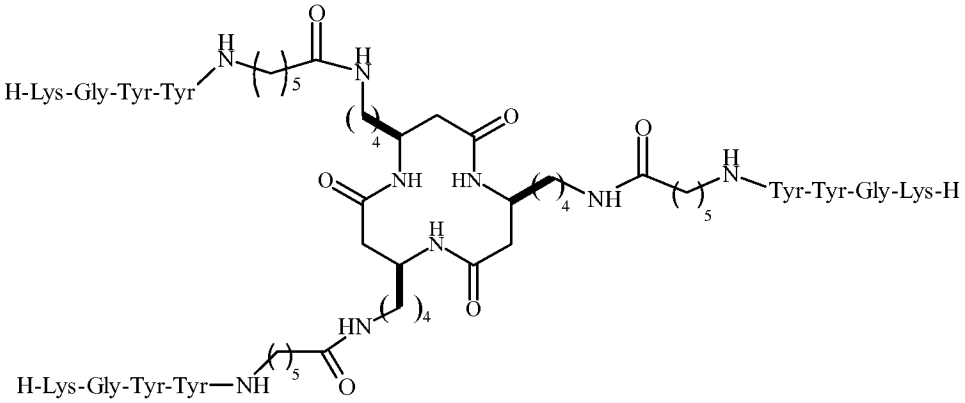


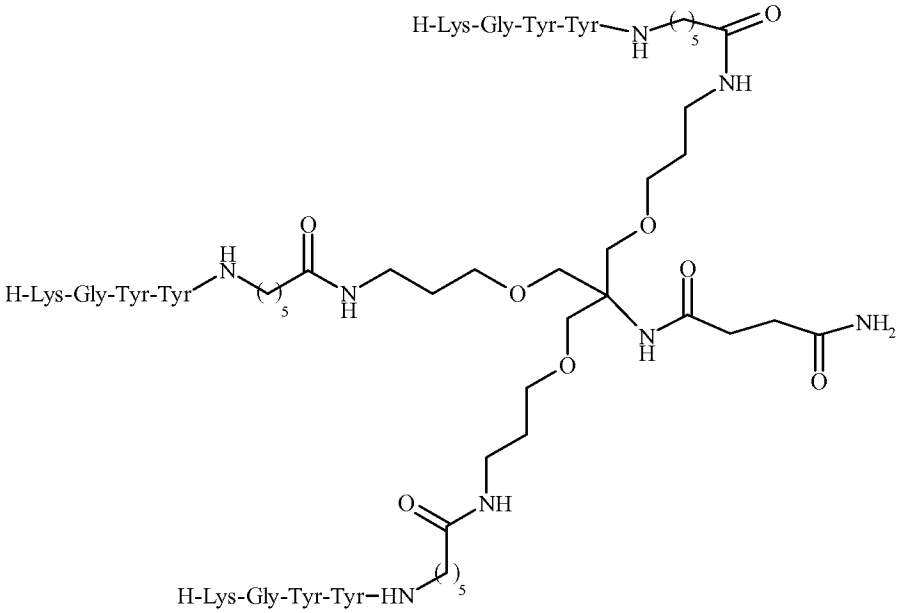
in which i represents an integer greater than or equal to 1.

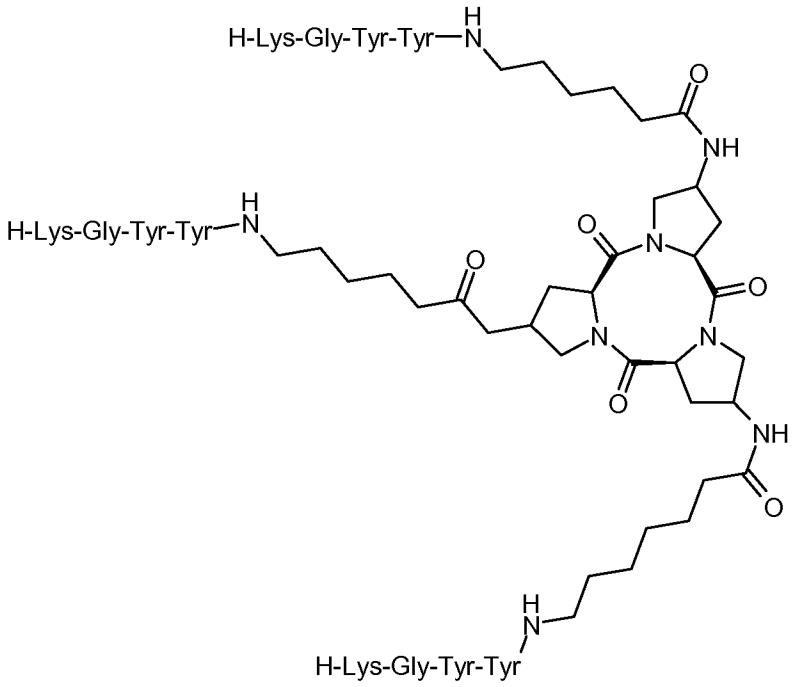
23. (previously presented) The molecule of claim 17, of the following formula (peptide sequence KGYY disclosed as SEQ ID NO: 3):

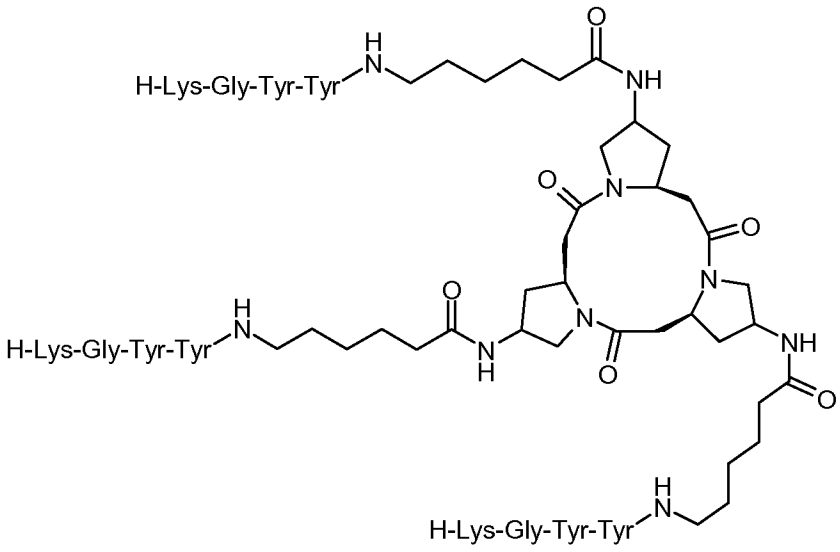




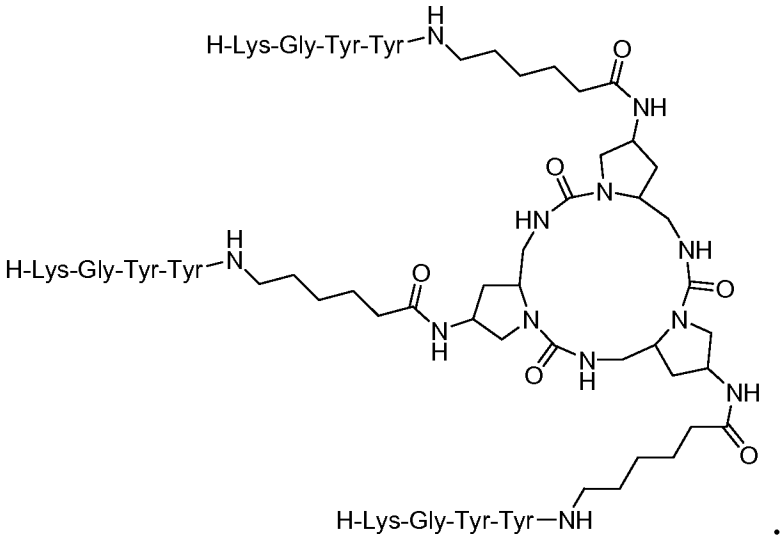

H-Lys-Gly-Tyr-Tyr
Tyr-Tyr-Gly-Lys-H
H-Lys-Gly-Tyr-Tyr—NH


H-Lys-Gly-Tyr-Tyr
H-Lys-Gly-Tyr-Tyr
H-Lys-Gly-Tyr-Tyr
H-Lys-Gly-Tyr-Tyr—HN


H-Lys-Gly-Tyr-Tyr
H-Lys-Gly-Tyr-Tyr
H-Lys-Gly-Tyr-Tyr


H-Lys-Gly-Tyr-Tyr
H-Lys-Gly-Tyr-Tyr
H-Lys-Gly-Tyr-Tyr

or



24. (previously presented) A pharmaceutical composition comprising, as active ingredient, a multimeric molecule according to claim 17, in combination with a pharmaceutically acceptable carrier.

25-28. (cancelled)

29. (Withdrawn – currently amended) A process for the preparation on a solid support of a multimeric molecule as defined in claim 21, in which A is a cyclic C_3 radical and corresponds to one of formulae Ia, Ib, II, VIb, VIc or VId ~~as defined in claim 21~~, said process ~~being characterized in that it comprises the following stages~~ comprising:

~~the formation of~~ forming a linear precursor of A~~, which precursor is constituted by~~ comprising an amino acid sequence forming a growing peptide chain, synthesized by successive coupling cycles between residues of N-protected amino acids~~, three of which~~

~~carry an R_a group of amine type,~~ and the amine function of the growing peptide chain, and deprotection, wherein three of the amino acid residues comprise an amine-type R_a group and the first amino acid residue ~~being~~ is attached to a solid support,

~~the cyclization of~~ cyclizing the ~~abovementioned~~ protected linear precursor of A,

~~the cleavage of said~~ cleaving the protective groups, in order to release ~~said~~ the protected amine functions,

~~the~~ coupling ~~of~~ the three released amine functions with an N-protected spacer arm B,

~~the deprotection of~~ deprotecting the spacer arm B and ~~the~~ coupling ~~of~~ the amine functions released from the spacer arm B, with a D peptide already formed or formed in situ by the sequential assembly of the amino acid residues corresponding to the D peptide, and

~~the cleavage of~~ cleaving the molecule from the solid support, after ~~the deletion of~~ deleting all the protective groups present on the functionalized side chains of the D peptide, in order to obtain the multimeric molecule.

30. (Withdrawn – currently amended) A process for the preparation in solution of a multimeric molecule as defined in claim 21, in which A is a cyclic C_3 radical and corresponds to one of formulae Ia, Ib, II, VIb, VIc or VId ~~as defined in claim 21~~, said process ~~being characterized in that it comprises the following stages~~ comprising:

~~the formation of~~ forming a linear precursor of A~~, which precursor is constituted by~~ comprising an amino acid sequence forming a growing peptide chain, synthesized by successive coupling cycles between N-protected amino acid residues~~, three of which carry an~~

~~amine-type R_a group,~~ and the amine function of the growing peptide chain, and deprotection, wherein three of the amino acid residues comprise an amine-type R_a group

~~the cyclization of~~ cyclizing the ~~abovementioned~~ protected linear precursor of A,

~~the cleavage of said~~ cleaving the protective groups, in order to release ~~said~~ the protected amine functions,

~~the~~ coupling ~~of~~ the three released amine functions with a -D-B peptide corresponding to a spacer arm B linked to a protected D peptide,

~~the deprotection of~~ deprotecting the protective groups present on the D peptide, in order to obtain the multimeric molecule ~~as defined in claim 1~~.

31. (Withdrawn – currently amended) A process for the preparation of a multimeric molecule as defined in claim 21, in which A is a branched C_3 radical and corresponds to one of formulae IV, V, VI or VIa ~~as defined in claim 21~~, said process ~~being characterized in that it comprises the following stages~~ comprising:

~~the~~ coupling ~~of~~ the three amine functions of the radical A of formula IV, V, VI or VIa with a protected spacer arm B,

~~the deprotection of~~ deprotecting the spacer arm B,

~~the assembly of~~ assembling the deprotected spacer arm B with protected amino acids involved in the constitution of a D peptide, by successive cycles of coupling, purification and deprotection of the ~~abovementioned~~ amino acids,

~~the deprotection of~~ deprotecting the last amino acid involved in the constitution of the D peptide, in order to obtain the multimeric molecule ~~as defined in claim 1~~.

32. (Withdrawn – currently amended) A process for the preparation on a solid support of a multimeric molecule as defined in claim 21, in which A is a non-symmetrical branched radical corresponding to one of formulae VII or VIII ~~as defined in claim 21~~, said process ~~being characterized in that it comprises the following stages~~ comprising:

~~the~~ grafting ~~of~~ a lysine onto a solid support, each of the two amino functions of the lysine, in positions α and ε ~~respectively~~, being protected by different and orthogonal protective groups ~~respectively~~,

~~the extension of~~ extending the peptide chain formed from the lysine, to the desired length, with successive couplings and deprotections,

~~* either of the amine functions in position α only, in order to obtain the radical A of formula VII, with protected amine functions in position ε,~~

~~* or of the amine functions in position ε only, in order to obtain the radical A of formula VIII, with protected amine functions in position α,~~

~~the~~ coupling ~~of~~ the deprotected amino functions in position ε in the radical A of formula VII or in α position in the radical A of formula VIII, with a protected arm B,

~~the assembly of~~ assembling the deprotected spacer arm B with a D peptide already formed or formed in situ by the sequential assembly of the amino acid residues corresponding to the D peptide, and

~~the cleavage of~~ cleaving the molecule thus obtained from the solid support, after ~~the deletion of~~ deleting all the protective groups present on the functionalized side chains of the D peptide, in order to obtain the multimeric molecule.

33. (previously presented) The molecule of claim 17, wherein each peptide derived from the ligand of the human or murine CD40 receptor (CD40L) is chosen from the following:

Arg-Ile-Tyr-Tyr (SEQ ID NO: 22),

Arg-Ile-Tyr-Tyr-Gly-Lys (SEQ ID NO: 23),

or from fragments of said peptides,

the amino acids being equally able to be of L or D-configuration.

34. (new) A method of treating lupus in a subject, comprising administering to the subject an effective amount of a multimeric molecule of claim 17.

35. (new) A method of treating lymphoma in a subject, comprising administering to the subject an effective amount of a multimeric molecule of claim 17.

36. (new) A method of treating parasitic infections in a subject, comprising administering to the subject an effective amount of a multimeric molecule of claim 17.

37. (new) The method according to claim 36, wherein said parasitic infection is Chagas' disease.

The following is an examiner's statement of reasons for allowance: The prior art of record does not teach or suggest, alone or in combination with any other art of record, the multimeric compounds claimed which bind to CD40 receptor. Further, new claims are supported by the specification examples and description.

As amended above, claims 17-24 and 29-34 are allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANDREW D. KOSAR whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654